37 C.F.R. § 1.132 DECLARATION TRAVERSING REJECTION

I, Ester Fernandez-Salas, declare that all statements made of my own knowledge are true. I also acknowledge that willful false statements are punishable by fine, imprisonment, or both under 18 U.S.C. § 1001 and that such willfully false statements may jeopardize the validity of any patent issuing from U.S. Patent Application 10/598,073 .

1. I am over the age of twenty-one, competent to testify in a court of law, and could and would testify to the matters set forth below before the United States Patent and Trademark Office.

2. I am a co-inventor in U.S. Patent Application 10/598,073.

3. I earned my Ph.D. degree in Biology and Biochemistry from the University of Girona, Spain in 1994; and my M.S. degree in Biochemistry and Molecular Biology from the Autonomous University of Barcelona in 1991. In the past 17 years as a research scientist in the fields of Cell Biology, Biochemistry, and Molecular Biology, I have authored peer-reviewed articles and book chapters, and made many public presentations, pertaining to molecular biology, protein chemistry, enzymology, and cell biology most recently in relation to the biological mechanisms and therapeutic uses of Clostridium botulinum neurotoxins.

4. Since 1994, I have worked continually in molecular biology, biochemistry, cell biology, and animal biology (both chemical and biological aspects).

   a. As a Fulbright Fellow I was engaged in post-doctoral research work from 1994-1996, in the fields of transgenic animal models for pancreatic cancer, cell biology of pancreatic cancer, and identification of regulatory sequences of pancreatic genes of interest.

   b. As a Fogarty Research Fellow at the NCI-NIH I was engaged in post-doctoral work from 1996-2000, in the area of skin cancer combining knock-out animal models, cell biology models, and molecular biology and biochemistry techniques to identify genes regulated by p53 and TNF-alpha involved in skin tumorigenesis.

c. I have worked continually in the biopharmaceutical field since 2000. During that entire time, my research has focused on botulinum neurotoxins, including the elucidation of the mechanism of action of the toxins and their long duration of effect.

d. I have worked in the Department of Biological Sciences at Allergan, Inc. for over 8 years and currently hold the title of Principal Scientist, Biology. In this position, I currently supervise 6 scientists engaged in developing cell based assays for botulinum toxins and in basic research to understand the mechanism of action of these toxins.

5. I have reviewed the September 22, 2008 USPTO Office Action for U.S. Patent Application 10/598,073 and the Examiner's comments and construed meanings for the terms "endogenous" and "exogenous." The Examiner asserts that the term "exogenous" means a portion of an FGFR3 that is located on the cell surface and the term "endogenous" means a portion of an FGFR3 that located within the cytoplasm. Described another way, the Examiner describes "exogenous" as an FGFR3 that is outside the cell membrane or a cell surface receptor that exists at a location that is exogenous to the cell cytoplasm. These asserted geographical meanings are incorrect interpretations that go against the well-established source of origin meaning of the term "exogenous" as used in the present application and as used by a person of ordinary skill in the relevant art.

6. Each cell of an organism comprises a genome that includes two copies of every gene from that organism. In cell biology, molecular biology and related fields, such a gene is referred to an "endogenous gene" because the gene was originally and naturally present in the cell's genome from its creation at cell division. A subsequently synthesized protein expressed from an endogenous gene is referred to as an "endogenous protein." In contrast, an "exogenous gene" is a copy of a gene that is introduced into the cell using recombinant biology techniques, such as, *e.g.*, transfection of a plasmid or viral-based expression construct. An exogenous gene is an extra copy because it is not one of the two copies of endogenous genes originally and naturally present in the cell's genome. An exogenous gene is introduced into the cell because this extra copy is not originally and naturally present in the cell, and as such, experimental manipulation of the cell is required in order to introduce this extra copy into the cell. The subsequently synthesized protein expressed

from an exogenous gene is referred to as an "exogenous protein". In addition, an exogenous protein can also be an external source of protein that is introduced directly into a cell using various protein transfection procedures. The purpose of introducing an exogenous gene is to express or over express the exogenous protein in the cell. As such, the terms "exogenous" and "endogenous" refer to the source of origin of the gene or protein and not to its geographical location in a cell. An endogenous gene/protein is one that is originally and naturally present in the cell, whereas an exogenous gene/protein is one that is introduced from an external source into the cell by experimental manipulation.

7. The Examiner's use of the terms "exogenous" and "endogenous" to refer to the geographic location of a FGFR3 is also contrary to the actual terms as used by a person skilled in the art to describe the cell surface domain and the cytoplasmic domain of a FGFR3, namely the extracellular domain and the intracellular domain. In cell biology, molecular biology and related fields, the term "extracellular" refers to a material that is present outside the plasma membrane of a cell, *i.e.*, the extracellular space. In contrast, the term "intracellular" refers to a material that is present within the cell, *i.e.*, the cytoplasm. Thus, the term of art used for referring to the portion of a protein present on the cell surface would be the "extracellular" portion, whereas the term of art used for referring to portion contained within the cytoplasm would be the "intracellular portion." In addition, a protein can have both intracellular and extracellular domains, such as, *e.g.*, a transmembrane protein like FGFR3.

8. In conclusion, the Examiner's asserted geographical meaning for the term "exogenous" to refer to a portion of an FGFR3 that is located on the cell surface and the asserted meaning for the term "endogenous" to refer to a portion of an FGFR3 that located within the cytoplasm is contrary to the well-established meaning of these terms as used in the present specification and in the relevant art.

Respectfully submitted,

Ester Fernandez-Salas. Ph.D.